

would endanger the regeneration and function of the iris, ciliary body and corneal endothelium.

## 2. Separation of tissue surfaces with a biological prosthesis

HUA can be used to separate tissue surfaces. The elastoviscous quality of HUA and its biological origin provide two advantages. First, it serves as a mechanical protector of the tissue during surgical manipulation and postoperatively; second, it does not cause inflammation, foreign body reaction, or development of a connective tissue capsule.

a. The use of HUA in retinal detachment surgery has two purposes. It provides the surgeon with a visco-elastic tool in the manipulation necessary for reattachment of the retina, and it facilitates the intraocular wound healing by preventing excessive fibrous tissue formation and development of intravitreal scar tissue (preretinal organizations, membranes, bands)<sup>(1)</sup>.

(1) Regnault et al., *Mod. Probl. Ophthal.*, Vol. 12, pps. 378-383 (1974); *Acta Ophthalmologica*, Vol. 49 (1971) pps. 975-6; Edmund, J., *Mod. Probl. Ophthal.*, Vol. 12, pps. 370-377 (1974).

b. The use of HUA as a biological prosthesis in the anterior chamber is indicated after cataract surgery in order to push back prolapsed vitreous and, after resection of the anterior face of the vitreous, to provide separation between the vitreous and cornea.

c. This biological prosthesis (HUA) can be used in the anterior chamber after keratoplasty to prevent adhesion formation between the corneal wound and the iris.

d. This biological prosthesis (HUA) can be used for the separation of tissue surfaces (endothelial or connective tissue) to promote fistula formation. When a new channel for liquid passage must be formed or a blocked channel has to be re-formed, the insertion of HUA jellies or dry membranes can help prevent the development of scar tissue during healing. Development of fistulae between the anterior chamber and subconjunctival space may be facilitated in this way in glaucoma surgery.

## 3. Protection of skin wounds

HUA can act as a barrier to water and microorganisms when it is used to cover extensive skin wounds caused by chemicals or heat. HUA in wet form or as a dry membrane, which becomes hydrated after contact with the wound, can provide effective protection against excessive water loss and can sieve out bacteria that do not have hyaluronidase activity.

Undoubtedly, other uses and applications of the ultrapure, non-inflammatory HUA of the invention might occur to those skilled in the art and thus, the foregoing brief description of the therapeutic uses of the HUA of the invention does not cover all the possible medical uses, nor does it intend to imply that in all the medical problems mentioned, HUA is, or will provide, the final remedy.

Variations and modifications can, of course, be made without departing from the spirit and scope of the invention.

Having thus described my invention what I desire to secure by Letter Patent and hereby claim is:

1. A sterile, pyrogen-free, protein-free, non-antigenic, hyaluronic acid fraction having an average molecular weight of at least about 750,000, a protein content of less than 0.5% by weight, ultraviolet light absorbance of a 1% solution of the sodium salt thereof of less than 3.0 at 257 nanometers wavelength and less than 2.0 at 280

nanometers wavelength, a kinematic viscosity of a 1% solution of the sodium salt thereof in physiological buffer of greater than about 1000 centistokes and a molar optical rotation of a 0.1-0.2% solution of the sodium salt thereof in physiological buffer of less than  $-11 = 10^3$  degree  $\text{cm}^2/\text{mole}$  (of disaccharide) measured at 220 nanometers; and which is characterized by infiltration by no more than about 200 white blood cells per  $\text{mm}^3$  of aqueous humor of the owl monkey eye when one milliliter of a 1% solution of the sodium salt of said fraction dissolved in physiological buffer is implanted in the vitreous replacing about one-half the existing liquid vitreous.

2. A fraction according to claim 1, wherein the molecular weight is at least about 1,200,000 and the kinematic viscosity is greater than about 10,000 centistokes.

3. The sodium salt of the hyaluronic acid fraction according to claim 1.

4. A method of improving pathological joint function in an animal by relieving pain, reducing inflammation and effecting the healing of an intraarticular wound associated therewith, said method comprising introducing by injection into an affected joint, an amount of hyaluronic acid according to claim 1, sufficient to increase the normal hyaluronic acid concentration in said joint by at least 5 times.

5. A method of enhancing normal joint and tendon function in an animal by lubricating said joint or tendon against excess stress during movement, said method comprising introducing into the synovial space associated with said joint or tendon an amount of the hyaluronic acid according to claim 1 sufficient to increase the normal hyaluronic concentration in said synovial space by at least 5 times.

6. A method according to claim 5, wherein the concentration is increased by a factor of 5 to 50 times.

7. A method according to claim 5, wherein said animal is a racing animal.

8. A method of preventing post-operative adhesion which may occur between healing tissues during the normal healing process, said method comprising introducing into a surgical site, either during surgery or post-operatively, an amount of the hyaluronic acid according to claim 1 sufficient to establish and maintain at the surgical site a hyaluronic acid concentration of at least about 1% for a period of about 24 hours post-operatively.

9. A method of separating healing tissues and maintaining said separation during the normal healing process after surgery, said method comprising introducing into a surgical site, either during surgery or post-operatively, an amount of the hyaluronic acid according to claim 1 sufficient to establish and maintain at the surgical site a hyaluronic acid concentration of at least about 1% for a period of about 24 hours post-operatively.

10. A method of protecting a layer of tissue during surgery on an adjacent layer of tissue, said method comprising introducing into the surgical site an amount of the hyaluronic acid according to claim 1 sufficient to prevent dislocation and movement of said tissue by providing a viscoelastic medium at the surgical site during said surgery.

11. A composition comprising the fraction according to claim 1 dissolved in a sterile physiological buffer solution containing NaCl,  $\text{Na}_2\text{HOP}_4 \cdot 7\text{H}_2\text{O}$  and  $\text{NaH}_2\text{PO}_4 \cdot \text{H}_2\text{O}$  in pyrogen-free double distilled water.

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